Periodical
WR

PUBLIC LIBRARY
MAR 8 1945
DETROIT

American Journal of Pharmacy

AND THE SCIENCES SUPPORTING PUBLIC HEALTH

DR. ROBERT P. FISCHELIS
Secretary and General Manager of the
American Pharmaceutical Association

Since 1825 *January, 1945*

Announcing . . . . . .

The Fifth Annual Seminar

on

Modern Pharmaceutical Practice

May 7, 8, 9, 1945

The purpose—

To give practicing pharmacists and other pharmaceutical graduates the opportunity to keep abreast of present-day advances in pharmacy.

Who may attend—

Any graduate of any recognized college of pharmacy.

Where it is to be held—

At the Philadelphia College of Pharmacy and Science.

When it is to be held—

Lectures commence Monday morning, May 7, 1945, and continue until Wednesday afternoon, May 9.

The cost—

An all-inclusive registration fee of $20 provides note book and comprehensive lecture outlines, and lunches for the duration of the seminar. Adequate rooming accommodations are available nearby at moderate rates.

The lecturers—

Members of the Faculty of the College will conduct all of the lectures, and demonstrations.

The scope—

The three-day period will be devoted to lectures, demonstrations and discussions on such topics as the microbiotics, amino acids, the newer antiseptics and insecticides, parenteral solutions, tropical diseases, the endocrines, sick room appliances and a number of miscellaneous drugs. There will be a question and answer period during which participants may have their own particular questions answered.

Send now for details.

Address the Registrar

Philadelphia College of Pharmacy and Science

43rd Street, Kingsessing and Woodland Avenues

Philadelphia 4 Founded 1821 Pennsylvania

THE STORY OF A *Clock*

The sturdy old clock in the factory tower looks down on industry and marvels at the great changes of the last several years. Everywhere industry is keeping step with each tick – not for 8 hours but round and round, day in and day out.

Following the first rumor of quinine shortage, there was set in motion the tremendous activity which brought about an eventual increase of 20,000% in the production of ATABRINE. This drug—often referred to as "yellow magic"—now gives antimalarial protection throughout the world to armed forces and to civilians of the United Nations.

Many other Winthrop preparations are also made on a "round the clock" schedule. Wartime needs are so stupendous, however, that even at this pace supplies are not always adequate for domestic needs.

When your order is not completely filled, bear with us—and please explain the reason for shortages to your patrons.

We thank you sincerely for your patience and understanding in the past.

WINTHROP CHEMICAL COMPANY, INC.

Pharmaceuticals of merit for the physician

170 VARICK STREET • NEW YORK 13, N. Y.

OVER fifteen million people see the new, dramatic, "Know Your Pharmacist Better" advertisements as they appear in the SATURDAY EVENING POST.

But even this tremendous audience can be multiplied many times over if you will display these striking advertisements on your counter where customers can see them.

On your counter, these Parke-Davis advertisements become *your* advertisements. They tell *your* customers about *your* professional services . . . explain why *you* won't sell sulfa drugs over-the-counter . . . give them a glimpse of the comprehensive prescription stock *you* maintain . . . show them the safeguards *you* place around the sale of laxative products.

If you have mislaid your copies of the POST for September 30, October 28, and December 16, send us your name and address and we will be glad to send you a set of reproductions of the first three ads, printed on heavy paper.

Parke, Davis & Company

DETROIT 32 • MICHIGAN

AND THERE WILL BE MORE OF THESE ADS IN THE POST DURING 1945!

AMERICAN JOURNAL OF PHARMACY

AND THE SCIENCES SUPPORTING PUBLIC HEALTH

Since 1825

LINWOOD F. TICE, Ph. G., B. Sc., M. Sc., Editor

Austin A. Dodge, Ph. C., B. Sc., Ph. D., Assistant to the Editor

John E. Kramer, B. Sc., Business Manager

COMMITTEE ON PUBLICATION

E. Fullerton Cook, P. D., Ph. M., M. S., Chairman

Mitchell Bernstein, P. D., M. D., F. A. C. P. — Louis Gershenfeld, P. D., Ph. M., D. Sc.

Marin S. Dunn, A. M., Ph. D. — John K. Thum, Ph. G., Ph. M.

J. W. Sturmer, Phar. D., Ph. M., D. Sc., Secretary

Ivor Griffith, P. D., Ph. M., D. Sc., F. R. S. A., ex officio

Vol. 117. JANUARY, 1945 No. 1

CONTENTS

PAGE

Our Cover:

Dr. Robert P. Fischelis 2

Editorial:

A. Ph. A. or C. I. O.? 3

Articles:

Bactericidal Efficiency of Iodine Solutions and Organic Mercurial Antiseptics. By L. Gershenfeld and G. W. Patterson, Jr. 5

Progress in the Conquest of Bacteria by New Medicinal Agents 12

Progress in the Conquest of Virus Diseases 20

Appetite and Walking Famine. By T. Swann Harding 27

The United States as the New Center for the Study of the History of Pharmacy. By H. Colle 35

Selected Abstracts 40

Book Reviews 43

Published monthly by the Philadelphia College of Pharmacy and Science 43rd Street, Kingsessing and Woodland Avenues, Philadelphia 4, Pa.

Annual Subscription, $3.00 — **Foreign Postage, 25 Cents Extra**

Single Numbers, 30 Cents — **Back Numbers, 50 Cents**

Entered as Second-Class Matter at the Post Office at Philadelphia, Pa. Under Act of March 3, 1879

Acceptance for Mailing at Special Rate of Postage Provided for in Section 1103 Act of October 3, 1917. Authorized February 15, 1920

OUR COVER

DR. ROBERT P. FISCHELIS

DR. ROBERT P. FISCHELIS, recently elected by the Council to be the Secretary and General Manager of the American Pharmaceutical Association, is one of the best-known men in American Pharmacy. For many years Dr. Fischelis has been active in the affairs of the A. Ph. A. and there is probably no one who better understands its organization and its aims as well as its several weaknesses. Furthermore, since the new Secretary has been a teacher, a college dean, a state board official, a state chemist, an editor, a member of a state board of health, the chairman of several joint professional committees and, finally, the director of an important Government agency in Washington, there is not a single aspect of pharmacy in which he has not had wide experience. Surely no broader background for this important position in pharmacy can be postulated and few indeed are those who could so qualify.

Those who know Dr. Fischelis are impressed by his boundless energy and forcefulness of purpose and these attributes have served the cause of pharmacy well on many past occasions. There are, of course, those who object to some of the policies and programs that the new Secretary instituted in the past but what forthright leader can avoid all criticism? It is obviously impossible to please each and every person in any field of human endeavor unless one is completely passive, does nothing, and never makes a positive statement.

Pharmacy has needed and needs dynamic leadership and it should be the obligation of every person in the broad field of pharmacy to support the new Secretary in his efforts to improve and strengthen the A. Ph. A.; only by such support can the progress which we need be achieved. As Americans the privilege to criticize that which we believe wrong is inalienable but this should not prevent us from supporting those duly chosen to represent our interests.

The AMERICAN JOURNAL OF PHARMACY pledges its support to Dr. Fischelis and we feel both hope and confidence in the future of our profession under his leadership.

E D I T O R I A L

A. PH. A. OR C. I. O.?

WE have pointed on several previous occasions to one of the greatest weaknesses in American pharmacy: the lack of a representative membership in the A. Ph. A. This condition has caused frequent embarrassment and disappointment to those who are charged with representing the interests of pharmacy to other professions and to government. How can our officers speak with authority for American pharmacists when they must admit that a very large percentage of those for whom they should speak neither support nor belong to the A. Ph. A.? In spite of this we hear every day petulant questions from disgruntled pharmacists asking why pharmacy isn't recognized here and why it is peremptorily dismissed there and why don't our leaders do something. Almost invariably these outspoken critics will admit on questioning that they do not belong to the A. Ph. A.

The wonder is that our position is as good as we find it, not that it isn't better. What has been accomplished has been done through the dogged efforts of a few self-sacrificing souls who in their struggles were laboring under conditions not unlike a ball team playing with their own home folks cheering for the other side.

The tremendous growth of labor organizations in this country has been phenomenal and no field of service has been immune from their organizers, not even pharmacy. It is not our wish to denounce labor organizations but rather to suggest and even insist that pharmacists if they wish to continue on a professional status cannot justify placing their affairs or future in the hands of an organization representing entirely non-professional vocations. Only by obtaining a truly representative membership in the A. Ph. A. and then *letting it protect our interests* can this be avoided. It would be wise for many executives in pharmaceutical industries, pharmaceutical organizations

and elsewhere to realize this and encourage those pharmacists on their staffs or within their spheres of influence to join the A. Ph. A. Instead of just opposing the union in a purely negative way something better should be offered. This alternative is and can be only the A. Ph. A.

Everyone who makes any effort at all to study the current trends of society knows that great and dramatic changes are taking place and will continue to do so. If we as pharmacists through neglect, complacency or sheer stubbornness fail to support our own organization then we must have no complaint if in the coming transition we lose our niche in the scheme of things. The A. Ph. A. has strong leadership and an ambitious program; it needs only our unanimous support.

L. F. Tice.

BACTERICIDAL EFFICIENCY OF IODINE SOLUTIONS AND ORGANIC MERCURIAL ANTISEPTICS*

By Louis Gershenfeld [1] and George W. Patterson, Jr.[2]

Introduction

IN 1873, Davaine discovered the antiseptic action of iodine. Reference to the use of the latter as an antiseptic in surgery is to be found in the fourth edition of the "Practice of Surgery" by Bryant (published in 1884). Willard in his "Annals of Surgery" (published in 1896), Senn in his "Surgery, Gynecology and Obstetrics" (published in 1905), and other prominent surgeons and scientists refer to iodine as the safest and most efficient of all antiseptics. For four decades, iodine has been prominently in the forefront as the antiseptic of choice for use as a skin disinfectant, particularly for the treatment of injuries and in surgical procedures. During this period, numerous antiseptics and bactericidal agents have been introduced, each bearing claims as the nearest approach to the ideal germicide.

Workers who in the past twenty-five or thirty years have had the task of testing and attempting to evaluate the bactericidal efficiency of different substances are familiar with the many obstacles which have been and still are facing them. Numerous procedures, methods and techniques have been introduced to determine the efficiency of disinfectants and antiseptics. Many advocate only laboratory (or *in vitro*) tests as a means of obtaining useful but also standardized methods for such evaluation. Other workers claim that clinical (*in vivo*) procedures are more satisfactory for this appraisal. The senior author has always advocated that where *in vitro* and *in vivo* tests are applicable, both should be employed, but in both instances conditions simulating practical use, as far as possible, should be followed. In most instances, *in vitro* tests are more easily performed and are less

* This investigation was conducted at the Philadelphia College of Pharmacy and Science, under a grant from the Iodine Educational Bureau's Industrial Fellowship at Mellon Institute.

[1] Professor of Bacteriology and Hygiene, Philadelphia College of Pharmacy and Science.

[2] Assistant Professor of Bacteriology, Philadelphia College of Pharmacy and Science.

costly than *in vivo* tests. It is obvious that, where findings obtained from a combination of *in vitro* and *in vivo* tests and interpreted in the light of practical use are such as to enable one to employ in the future the findings from the *in vitro* tests alone as a means of evaluating the efficiency of the same antiseptics, there could be no objection to such procedure.

In 1932, a report from our laboratories on the bactericidal efficiency of iodine solutions (1) revealed that "3% solutions of iodine were found to be superior to any of the other commonly used bactericidal agents in the dilutions most frequently employed." This conclusion was reached after comparing by *in vitro* methods many iodine solutions with mercurials and other antiseptics. Since this report numerous *in vivo* methods have been proposed. In these different procedures as well as in combinations of *in vitro* and *in vivo* tests, the findings as to the efficiency of iodine were usually similar to that reported by our laboratory (2) where the toxicity displayed by iodine was less than that of other antiseptics, especially the mercurials, silver salts and the halogens.

Purpose of Investigation

It may be possible to correlate the bactericidal efficiencies and tissue toxicities of the various antiseptics, but such a correlation would not be satisfactory without considering other conditions in clinical practice, such as dilution by blood, serum, mucus, exudate, inhibition of penetration by the formation of metallic albuminates or other precipitates, incompatibility with body fluids and other interferences. With this fact in mind and with the knowledge that thioglycollate medium inactivates or neutralizes the antiseptic action of many substances, or neutralizes the bactericidal and bacteriostatic action of many substances, thus more closely paralleling conditions in practical disinfection, the following *in vitro* investigation was conducted so as to evaluate under the conditions of the methods of testing the bactericidal efficiency of iodine solutions with that of organic mercurial antiseptics in common use.

Antiseptics Used

Iodine Solutions

1. Liquor Iodi (Solution of Iodine), U. S. P. Assay revealed 1.94% free iodine.

2. Liquor Iodi Fortis (Lugol's Solution), U. S. P. Assay revealed 4.94% free iodine.

3. Tincture Iodi (Tincture of Iodine), U. S. P. Assay revealed 6.93% free iodine.

4. Tincture Iodi Mitis (Mild Tincture of Iodine), U. S. P. Assay revealed 1.94% free iodine.

Organic Mercurial Solutions

A. Proprietary organic mercurial solution, aqueous, 1:1000, containing a surface tension reducing agent and buffered to isotonicity, the basic compound containing approximately 45 per cent of mercury.

B. The basic compound was the same as that present in (A) containing the surface tension reducing agent dissolved in a mixture containing alcohol, 47.5%; acetone, 10%; water, q. s.

C. Proprietary organic mercurial solution, 1:500, dissolved in water by means of sodium hydroxide to form the sodium salt, the basic compound containing approximately 56 to 57 per cent of mercury.

D. The basic compound was the same as in (C) but this was dissolved in a mixture containing alcohol, 47.5%; acetone, 10%, and water q. s.

E. Proprietary organic mercurial solution, 2%, dissolved in a slightly alkalized mixture of alcohol, 52.2%; acetone, 10%; water, q. s., the basic compound containing approximately 25 per cent of mercury and 20 per cent of bromine.

Note: All the proprietary organic mercurials (A, B, C, D and E) were obtained on the open market in original unopened containers in the concentrations as given.

1. Iodine Solutions

Procedure:

Temperature of test: 20° C.

Test organisms: Standard F. D. A. strains of *Staphylococcus aureus* and *E. typhosa.*

Transplant medium: Thioglycollate medium.*

* Fluid thioglycollate medium (Brewer). Formula in Memorandum issued by National Institute of Health on December 30, 1941, and in Gershenfeld's Bacteriology and Allied Subjects, 1945, p. 75.

Technique: One cc. of the respective iodine solutions was mixed separately with 1, 2, 3 and 5 cc. and then by increments of 5 cc. (10, 15, 20, 25, 30, 35, 40 cc.) of broth cultures of the respective test organisms. The mixtures were kept at 20° C. and a standard 4 mm. loopful was transplanted into 10 cc. of thioglycollate medium at intervals of 1, 2, 3, 4, 5, 10 and 15 minutes. The transplants were incubated at 37° C. for 4 days.

Findings:

All iodine solutions including the 2% iodine solution (in 1 cc. amounts) were effective within 1 minute against 25 cc. of broth cultures of the above organisms when tested as above.

Note: It will be observed that 5 cc. of the respective mercurials were used in the same techniques (see below), owing to the ineffectiveness of some of them in 1 cc. amounts. In the same proportion, for purposes of comparison, 5 cc. of the 2% and other iodine solutions were effective within 1 minute against 125 cc. of broth cultures of the respective test organisms.

2. Organic Mercurials

Procedure:

All conditions were the same as under Iodine Solutions (see (1)), except that 5 cc. of the mercurials were used instead of 1 cc.

Findings:

Five cc. of the proprietary product (A) were not effective at 20° C. against 0.5 cc. of either *Staphylococcus aureus* or *E. typhosa* within 15 minutes.

Five cc. of proprietary product (B) were effective against 5 cc. of a broth culture of *E. typhosa* within 1 minute, but 15 minutes were required for *Staphylococcus aureus.* This quantity was effective against 2 cc. of a broth culture of *Staph. aureus* within 1 minute. It was effective against 10 cc. of a broth culture of *E. typhosa* within 3 minutes, but *Staph. aureus* was not killed within 15 minutes. It was not effective against larger amounts of the broth cultures of the test organisms within a 15-minute period.

Five cc. of proprietary product (C) were not effective at 20° C. against 0.5 cc. and larger amounts of a broth culture of *Staph. aureus* within 15 minutes. It was effective against 5 cc. of a broth culture of *E. typhosa* within 3 minutes but not against larger amounts within that time period.

Five cc. of proprietary product (D) were effective against 10 cc. of a broth culture of *E. typhosa* within 1 minute but required 5 minutes for 20 cc. of culture. It was effective against 2 cc. of a broth culture of *Staph. aureus* within 1 minute but required 5 minutes for 5 cc. of culture. It was not effective against larger amounts of *Staph. aureus* within 15 minutes.

Five cc. of proprietary product (E) were effective against 10 cc. of a broth culture of *E. typhosa* within 1 minute but it was not effective against 20 cc. or larger amounts within 15 minutes. It was effective against 2 cc. of a broth culture of *Staph. aureus* within 1 minute; it required 10 minutes for 5 cc. of culture; and it was not effective for larger amounts within the 15-minute period.

3. Iodine Solutions

Procedure:

Test organisms and
Temperature of test: 20° C. for *E. typhosa;*
37° C. for *Staph. aureus.*

Transplant medium: Thioglycollate medium.

Technique: Five cc. of varying dilutions of the Iodine Solutions were mixed separately with 0.5 cc. of a broth culture of the respective test organisms. The mixtures were kept at the respective temperatures and a standard 4 mm. loopful was transplanted into 10 cc. of thioglycollate medium at intervals of 5, 10 and 15 minutes. The transplants were incubated at 37° C. for 4 days.

Findings:

The 2% aqueous solution was effective against *E. typhosa* within 5 minutes in a 1:300 dilution. The 2% tincture was effective in a 1:325 dilution.

The 7% tincture was effective in a 1:800 dilution within 5 minutes.

The 2% aqueous iodine solution and the 2% tincture of iodine were effective against *Staphylococcus aureus* within 5 minutes in a concentration of 1:150. The 7% tincture was effective in a 1:500 dilution within 5 minutes.

4. Organic Mercurials

Procedure:

All conditions were the same as under Iodine Solutions (see (3)).

Findings:

Proprietary product (A) was not effective against *E. typhosa* and *Staphylococcus aureus* within 15 minutes.

Proprietary product (B) was effective against *E. typhosa* within 5 minutes in a 1:3 dilution. The lowest concentration which killed *E. typhosa* and also *Staph. aureus* within 15 minutes was a 1:4 dilution. Against *Staph. aureus* a 1:3 dilution was effective within 5 minutes.

Proprietary product (C) was effective against *E. typhosa* within 5 minutes in a 1:3 dilution. Against *Staph. aureus* it was effective only undiluted within 15 minutes.

Proprietary product (D) was effective against *E. typhosa* within 5 minutes in a 1:5 dilution. Against *Staph. aureus* a 1:3 dilution was effective within 5 minutes.

Proprietary product (E) was effective against *E. typhosa* within 5 minutes in a 1:5 dilution. Against *Staph. aureus* a 1:3 dilution was effective within 5 minutes.

Summary and Conclusions

Bactericidal efficiency tests were conducted comparing the U. S. P. Iodine Solutions with some of the marketed proprietary organic mercurial antiseptics.

The tests conducted took into consideration two important factors. In the first instance, the undiluted antiseptics remained constant and the varying factor was the increased amounts of broth cultures of the test organisms. In this manner the antiseptic became diluted and there was constantly added increased amounts of organic matter and bacteria. The temperature employed was 20° C., approximating that of the room environment which in turn seems more satisfactory for

comparing the efficiency of antiseptics used externally where the time factor is a very short period. In all instances transplants were made into thioglycollate medium, which served also to neutralize or inactivate any of the antiseptic which might have been carried over from the mixture of medicament and organisms. Our findings prove this to be the case, for where transplants were made into F. D. A. media, all other conditions being identical, the findings revealed more satisfactory results in favor of the respective antiseptics, especially the mercurial compounds. In this technique using thioglycollate medium, all Iodine Solutions, including the 2% Iodine Solutions, were effective within one minute using 1 cc. of each of these Iodine Solutions against 25 cc. of broth cultures of standard (F. D. A.) strains of *Staph. aureus* and *E. typhosa*. None of the proprietary organic mercurials tested revealed findings approaching this effectiveness. Proprietary product (A) was not effective even against 0.5 cc. of either organisms within 15 minutes. Proprietary product (B) in 5 cc. quantities was more effective than the proprietary product (A) but did not approach the Iodine Solutions in effectiveness as indicated above. In like manner, the proprietary organic mercurials (C), (D), and (E) did not approach (in 5 cc. quantities each) the Iodine Solutions in effectiveness as indicated above.

In the other series of tests the technique used was the F. D. A. Phenol Coefficient Test. The only difference was that transplants were made into thioglycollate medium instead of F. D. A. broth. As will be noted from the findings above, the highest dilution of any of the proprietary organic mercurials tested which was effective within five minutes against *E. typhosa* was a 1:5 dilution, and against *Staph. aureus* it was a 1:3 dilution. The Iodine Solutions in the same period of time using for comparison the weakest Iodine preparation, the 2% aqueous Iodine Solution, were effective within five minutes against *E. typhosa* in a 1:300 dilution and against *Staph. aureus* in a 1:150 concentration.

The above comparative values show the markedly greater bactericidal efficiency of Iodine Solutions as compared with the proprietary organic mercurial antiseptics employed in this study.

REFERENCES

(1) Gershenfeld, L., and Miller, Ruth E.: *J. A. Ph. A. 21*, 894 (1932).
(2) Witlin, B.: *Amer. Jour. Pharm. 113*, 353 (1941).

PROGRESS IN THE CONQUEST OF BACTERIA BY NEW MEDICINAL AGENTS *

By Chester S. Keefer **

THE patient was a young woman who gave birth to her third baby. For the first four days she was well; then suddenly she had a chill, which was immediately followed by high fever. Almost at once, there were signs of a spreading peritonitis, and within a week she was dead. Hemolytic streptococci were found in her uterine discharges on the fifth day and in her peritoneal cavity after death. This was in 1935—nine years ago.

A second patient, also a young woman, had just given birth to her second baby. For the first three days she remained well; then suddenly she had a chill, high fever, the signs of peritonitis, and bacteremia due to the hemolytic streptococcus. She was given sulfanilamide at once. Within 48 hours the temperature was lower, the organisms had disappeared from the blood, and within ten days after the onset of the signs of acute infection she was well. This was in 1937, only 7 years ago.

The third patient, also a young woman, was showing all the signs of puerperal fever which was being treated intensively with one of the sulfonamides. The effects were of a transitory nature in that the disease process had continued for 10 days in spite of large doses of the drug. Penicillin was then substituted for the sulfonamides and within 10 days after it was started this woman was well. This was in 1942—two years ago.

The story of these three patients illustrate what has been accomplished in the treatment of childbed fever in the past nine years. In a 5-year period before sulfanilamide, Leonard Colebrook found that the death rate in all cases of childbed fever due to the hemolytic streptococcus was 22.6 per cent. After sulfanilamide was begun, the mortality fell to 5.5 per cent—one-quarter of the former figure. This

---

* Address at Scientific Award Ceremony of American Pharmaceutical Manufacturers' Association, at Waldorf-Astoria in New York, on December 11, 1944.

** Doctor of Medicine, Wade Professor of Medicine, Boston University School of Medicine.

was the first clear demonstration of what the sulfonamides could do in puerperal fever. We know now that penicillin will influence in a favorable sense many of the cases of hemolytic streptococcic infections in which the sulfonamides have failed.

In the conquest of bacterial infections, we have made remarkable progress and we have traveled a long way on the road to achievement. The three cases I have just cited illustrate the trend, but that is not all. Today, I want to review some of the highlights of the past few years in this rapidly moving narrative of chemotherapy in bacterial infections. I shall confine my remarks to the progress resulting from the discovery and application of the sulfonamides and penicillin.

The great love of man for magic has stimulated physicians for many years to look for "magic bullets," that might be shot into the body and directed to the affected part. Here, these bullets would attack an infection by eliminating or destroying it without injuring the body itself. While the great possibilities of chemotherapy have been known for some years, this new branch of science has lacked effective support until recently. Until 10 years ago, progress in this field was exceedingly slow. With the discovery of the usefulness of the sulfonamides in the treatment of disease, there has been a remarkable acceleration in the field of chemotherapy.

Chemotherapeutic and Chemoprophylactic Agents in Hemolytic Streptococcic Infections

It is well worth recalling that the sulfonamides were tested first in hemolytic streptococcal infections. The results which were obtained in puerperal sepsis, and in meningitis, soon resolved any doubts that were in the minds of those who questioned its therapeutic value. I have already said that the fatality rate was reduced to one-fourth of its previous rate in puerperal sepsis; in streptococcal meningitis, which was almost always invariably fatal, the case fatality rate was reduced to about 40 per cent. In those instances of infection which are associated with a lower fatality rate, the course of the disease was shortened and the incidence of complications has been reduced.

It is unnecessary to say that this group of microorganisms is among the most important of all disease-producing agents. As a result of surveys by the U. S. Public Health Service, we are told that

in many civilian communities the hemolytic streptococcus is responsible for 5 per cent of all measurable illness, and at least 20 per cent of all bacterial infections of the respiratory tract. In the Army and Navy, hemolytic streptococcal infections rank extremely high as a cause of illness and disability. Aside from the damage it produces in the respiratory tract, this group of organisms may invade any organ of the body and produce serious disease.

Great strides have been made in both the prophylaxis and treatment of all streptococcal diseases. I want to tell you about some of the recent successes that have been obtained by the Naval Medical Corps working under the direction of the Division of Preventive Medicine of the Bureau of Medicine and Surgery. The experience which they record has been large and the results have been convincing. More than 600,000 men received daily doses of sulfadiazine for a period of 6 months to test its protective power against respiratory diseases. It was demonstrated "that chemoprophylaxis was 85 per cent effective in preventing bacterial infections of the respiratory tract under conditions which were favorable for the dissemination of respiratory pathogens and unfavorable to newly inducted recruits." It was estimated that in a center of 30,000 recruits one can anticipate a saving of 30,000 hospital days each month during seasons when respiratory diseases are prevalent. This is equivalent to freeing a 1000-bed hospital and all the labor and personnel associated with the care of the sick. The most striking reduction occurred in hemolytic streptococcic infections such as scarlet fever, tonsillitis, pharyngitis, suppurative infections and rheumatic fever. Primary streptococcic pneumonia was eliminated and meningococcic meningitis was extremely rare. The incidence of virus infections such as measles and mumps was not decreased. While the attack rate from pneumococcus pneumonia was decreased, the morbidity rate remained high. Thus, it has been demonstrated that the sulfonamides are effective prophylactic agents in many diseases of the respiratory tract and in particular those due to the hemolytic streptococcus and meningococcus.

Pneumonia

Following the discovery of sulfanilamide, it was a great disappointment to find that it had no beneficial effect on pneumococcus lobar pneumonia. I say it was a disappointment because for years

many students of this disease had been searching for more effective therapeutic weapons. Only partial success had been achieved. By using type specific serum the average fatality rate had been cut in half, but there were many difficult problems remaining. It was only 2 years after the development of sulfanilamide for medicinal uses that a derivative was discovered in sulfapyridine. This drug was effective against the pneumococcus. Its discovery was soon followed by others so that we have at the present time at least 5 sulfonamide derivatives which are effective against this disease. Let me tell you what the life insurance companies have to say about the fatality rate from pneumonia in the pre- and post-sulfonamide days.

Underleider, Steinhaus and Gubner comment on the experience of the Equitable Life Assurance Society of the United States. An analysis of their experience with pneumonia among large groups of industrial employees carrying group health and life insurance was made, and a comparison between the pre-sulfonamide years 1935-1937, and the period from January, 1939 to 1942 was noted.

In this short period of time, there was a reduction in the case fatality rate from an average of 20.8 per cent to 3.9 per cent—one-fifth of the former rate. Also, it was significant that there was a decrease in the total duration of illness from the most frequent period of 38 days in 1935 to 27 days in 1941. It was calculated, therefore, that the advent of sulfonamide therapy has proved a boon to industry, in saving at least some twenty-five thousand workers annually. A further annual saving of over a million working days has resulted from the shortening of the period of illness. This is an impressive record, and requires no comment.

It might be added, however, that the fatality rate in pneumonia in the general population between the ages of 15 and 65 is now of the order of 4 per cent. I have been informed of one series of 1300 cases of lobar pneumonia in a single military camp without a single death. One needs no further testimony to convince even the most skeptical about the value of the sulfonamides in pneumococcus pneumonia.

It is a great privilege to have witnessed a period when for years there was no specific treatment for pneumonia, then a period when specific serum for a few specific types reduced the fatality rate by half, and finally a period of chemotherapy when the fatality rate has been reduced to one-fifth of its former rate. It may be added that

penicillin is as effective as the insulfonamides, and it may have a favorable effect in some cases when the sulfonamides have failed.

Meningococcus Meningitis

Before the days of the sulfonamides the fatality rate in this disease, which occurs either sporadically or in epidemic form, was in the neighborhood of 40 per cent. Now, it is less than 5 per cent. It is also firmly established as a result of the investigations of the Army Epidemiological Board that carriers of meningococci can be rendered free of organisms within 48 to 72 hours with only 1 gram of sulfadiazine a day. Recent studies in our Navy have demonstrated that men on prophylactic doses of sulfonamides rarely acquire this disease. You will agree with me that this achievement is one of great moment and importance in both civilian and military medicine.

Dysentery

One of the soldier's greatest enemies is dysentery. It was bacillary dysentery and not the Turk that drove the British out of Gallipoli during the last war. In this campaign, at least 100,000 casualties were due to dysentery. At one time, during this war, dysentery was a greater threat to the capture of Port Moresby by the Japanese than any other factor. The sulfonamides aided enormously in saving the day. The average fatality rate for dysentery has varied in the past from 10 to 50 per cent, depending upon the type of dysentery and other associated conditions. In those patients recovering, the average number of days of treatment in a series of 2000 patients in the British Army in 1917-1918 was one hundred and forty-one days—and what days they were for many of the victims of dysentery. A German soldier of that time wrote that "dysentery dissolves our bowels; the latrines are densely crowded; the faces are grey, yellow, miserable and wasted, and from the bodies of these bent figures the colic wrings out the blood. With trembling lips, distorted with pain, some grin at one another and say, 'It's not much sense pulling up one's trousers again.'"

But all of this is changed with the use of the sulfonamides. The fatality rate in bacillary dysentery at present is less than one-half of 1 per cent, and the average number of hospital days for its victims has been between 14 and 16 days. The acute symptoms have frequently disappeared within 72 to 96 hours—a phenomenal change indeed.

Venereal Diseases

The sulfonamides were surprisingly effective in the treatment of gonococcal infections, and the results were far superior to any other previous form of treatment. This was also true when they were used as prophylactic agents. There were some failures, but the use of the sulfonamides changed the course of this disease in a most extraordinary way.

In addition to these infections, the sulfonamides have been of great value in the treatment of infected wounds and burns. Invasive infections have been reduced and the fatality rate is exceedingly low. Urinary tract infections are influenced favorably. The fatality rate in cases of influenza bacillus meningitis is reduced when the sulfonamides are combined with serum.

Thus, we can say that the sulfonamides have made a tremendous difference in the outlook of infectious diseases. Their scope and limitations have been fairly well defined. They have saved many lives, many days of illness and much suffering. Their discovery served to stimulate investigation in the field of chemotherapy at an unprecedented pace.

In 1941, we were all aware of the fact that the sulfonamides were of little value in the treatment of staphylococcic infections. This was a serious matter, because the staphylococcus is the commonest organism in wound infections, and it causes many cases of acute and chronic diseases of a serious nature. It was at this time that interest was aroused in penicillin, the greatest of all chemotherapeutic agents so far discovered.

The story of its discovery and development is one of the most remarkable in modern day science. Indeed, the development of the knowledge of its therapeutic power, its production and distribution, is a unique example of collaborative efforts—scientific, industrial and administrative. This story is not unknown to your Association. Your award of distinction to Professors Fleming and Florey in 1943 is expert testimony of your appreciation of the significance of penicillin in the field of chemotherapy. The reason penicillin is such a remarkable agent is due to two facts: it is powerful and effective in many different diseases, and it is non-toxic.

It is a really "magic bullet" with tremendous power to destroy bacteria without destroying or damaging tissue. For example, one milligram of crystalline penicillin (or 1666 units) will inhibit the

DETROIT PUBLIC LIBRARY

growth of staphylococci in 82 liters of nutrient broth. Thirty milligrams are adequate to cure most cases of gonorrhea within 24 hours. Let me recall briefly what can be accomplished with this agent in the treatment of infections.

It is the most effective chemotherapeutic agent in all of the infections due to gram positive organisms, including the staphylococcus, hemolytic streptococcus, pneumococcus, the gas bacillus, and the anthrax bacillus. It is truly extraordinary that it is effective against both syphilis and gonorrhea. Certainly it is the best drug available for the treatment of such diverse diseases as pyogenic meningitis, bacterial endocarditis, mastoiditis, empyema, lung abscess, and bronchiectasis, acute and chronic osteomyelitis, and infected wounds and burns.

The value of penicillin in military medicine and surgery cannot be fully assessed at the present time. A recent citation upon the occasion of the award of the Legion of Merit to Major Champ Lyons is pertinent. "He initiated and guided the methods by which the new and potent agent penicillin has been utilized in the seriously wounded. From the most forward mobile hospitals in Italy to the large general hospitals of the interior he has personally operated on and studied the treatment of the wounded . . . Lives and limbs of soldiers have been saved and the disability and deformity of wounds materially reduced."

In essence, there is no other chemotherapeutic agent known that can do much with so little for so many diseases. When we stop to consider that 2 years ago less than 50 patients had received penicillin and that today there is an adequate amount for our armed forces and for those of our allies, and a moderate supply for civilians, it is a great tribute to collaborative efforts. The mobilization of all forces to bring this about is one of the unique accomplishments in medical research. Your industry deserves high praise for the magnificent part it has played in its development.

What is the outlook for the future? The present period has been called the golden age of therapeutics and chemotherapeutic agents have proved their value in the control of many infections. The way is now open for the continuation of research and development in this most important field. In this country, there is no lack of imagination, there is no shortage of workers with a high capacity for original thought, and material resources are not lacking to give them the

support which is needed to bring this thought to full maturity. But there is much that remains to be done. We recognize that there are no effective chemotherapeutic agents against virus diseases, nor against the tubercle bacillus. Many of the gram negative organisms resist the action of all agents. We need better chemotherapeutic agents for the parasitic, and for many of the insect borne diseases. The problems continue to be numerous. However, we have every reason to hope that new agents will be found which will be effective against infectious diseases which continue to thrive in the face of our present medicinal agents.

In the conquest of bacterial infections, the collaborative efforts of the pharmaceutical industry and medicine have been outstanding. That these cooperative efforts will continue there is no doubt. Each has something to contribute to a common objective. Let this objective be the advancement of medical science for the purpose of better health.

PROGRESS IN THE CONQUEST OF VIRUS DISEASES*

By W. M. Stanley **

VIRUSES are small infectious agents that can cause disease in man, other animals, plants and bacteria. They range in size from about 10 mu, or a size slightly smaller than that of certain protein molecules, in an almost continuous spectrum of sizes up to about 300 mu, or a size slightly larger than that of certain accepted living organisms. A given virus can multiply and cause disease only when within the cells of certain specific living organisms. No virus has been found to reproduce in the absence of living cells. During multiplication viruses occasionally change or mutate to form a new strain which in turn causes a new disease. Viruses were not discovered until 1892 when Iwanowski demonstrated that the causative agent of the mosaic disease of tobacco would pass through a filter that retained all known living organisms. Six years later Beijerinck proved that this agent was not an ordinary living organism and recognized it as a new type of infectious disease-producing agent—namely, a virus. The same year Loeffler and Frosch demonstrated that foot-and-mouth disease of cattle was caused by a virus. The discovery of the first virus disease of man, that of yellow fever, was made in 1901 by Reed and co-workers. Since then over two hundred diseases of man, other animals and plants have been found to be due to viruses. Among such diseases are small pox, measles, poliomyelitis, St. Louis encephalitis, influenza, virus pneumonia, fever blisters, equine encephalomyelitis, rabies, hog cholera, dog distemper, fowl pox, jaundice of silkworms, tumorous growths in fowls and in other animals, various yellows and mosaic diseases of plants and the transmissible lysin of bacteria.

The agents responsible for these and other virus diseases are characterized by their small size, by their ability to multiply only within the cells of specific living hosts and by their tendency to mutate or change. Because properties such as reproduction and muta-

---

* Address at Scientific Award Ceremony of American Pharmaceutical Manufacturers' Association, at Waldorf-Astoria in New York, on December 11, 1944.

** Member of the Rockefeller Institute for Medical Research, Princeton, N. J.

tion have long been regarded to be characteristic of living entities, viruses were, for many years, regarded as living organisms somewhat smaller than ordinary bacteria. However, the isolation in 1935 of tobacco mosaic virus in the form of a crystalline nucleoprotein of unusually high molecular weight and the subsequent isolation of still other viruses in the form of high molecular weight proteins, some of which were also crystallizable, cast doubt upon the validity of classifying all viruses as organisms. With the exception of virus activity, the properties of some of the smaller viruses are quite similar to the properties of ordinary protein molecules, whereas at the other extreme, with respect to size, the properties of the viruses are more nearly like those of accepted living organisms. The viruses, therefore, serve as a bridge between the molecules of the chemist and the organisms of the bacteriologist, and provide us with new reasons for considering that life as we know it, owes its existence to structure, to a specific state of matter and that the vital phenomenon does not occur spontaneously, but is possessed in varying degrees by all matter. This phase of viruses cannot be developed at this time, for today we must be interested in viruses as disease-producing agents.

The almost miraculous results that have been obtained during the past few years with the sulfa drugs and with penicillin in the treatment of infectious diseases caused by bacteria, bring into bold relief the fact that these same wonder materials are almost without effect in the treatment of diseases caused by viruses. This fact can be regarded as an indication that the mode of action of viruses differs fundamentally from that of bacteria. Since practically nothing is known of the mechanism of virus reproduction, an attack, at the present time, on virus diseases from the standpoint of chemotherapy, will have to be more or less empirical in nature. Fortunately, however, progress has been made in the conquest of virus diseases, although made, not as a counterpart of modern advances in the conquest of bacterial diseases, but rather as a result of the application of two basic procedures, one of which became established empirically at least three thousand years ago and the other of which was probably used by Pasteur in 1884. It is paradoxical that these two basic procedures were known long before the discovery of viruses as such and that during the intervening years no fundamental improvement has been made.

About three thousand years ago, at a time when disease was generally regarded as being due to evil spirits or to the will of the gods,

it was known that the application of the dried scabs or the contents of pocks and pustules from a person suffering from small pox, to the lightly scarified skin of persons who had never had the disease, resulted many times in only a mild reaction. These persons were then protected against the more severe disease, small pox. Scabs or material from the sites of the mild reactions could be applied to still other persons, usually with good results. It seems likely that the small pox virus was modified by the repeated skin passage in man and that here we have the first example of the modification or mutation of a virus and the use of the new virus strain for purposes of immunization. During the ensuing years occasional references were made to artificial variolation as a means of protection against small pox, for the method was used from time to time for the immunization of royal personages, yet it was not until 1798 that a definite method of immunization against small pox was formally advocated. In that year Jenner reported that lymph tissue from cows suffering from cow pox could be used to vaccinate or protect man against small pox. Although the method was still purely empirical, Jennerian vaccination came into general use throughout the civilized world and is used to this day. The first basic procedure consists, therefore, in the inoculation of a vaccine containing active virus, the virus usually first having been modified by passage in an unnatural host. Although variations of this procedure have been introduced, such as, for example, the inoculation of unmodified virus by an unnatural route or the inoculation of unmodified virus simultaneously with immune serum, the essential immunity which results is due in all cases to the active virus that is produced in the host. Because of the tendency of viruses to change or mutate during reproduction, the possibility always exists that an unwanted strain of virus may arise during the production of the virus; hence, it is obvious that such active vaccines must be tested continuously to be certain that they do not contain undesirable viruses or virus strains.

The conquest of yellow fever is the outstanding modern example of the application of this basic method for the control of a human virus disease. The earlier history of the United States is replete with harrowing descriptions of the ravages caused by this virus disease, and until recently there was no means of immunization against yellow fever. Fortunately, in 1930 Theiler reported that yellow fever virus could be altered by passage in mouse brains. Later the virus was

further modified by passage in tissue culture so that a strain, known as 17 D, was evolved, which was found useful for human vaccination. The use of this vaccine plus adequate mosquito control measures have resulted in the elimination of yellow fever as a major public health problem in the Americas and in Africa. During the year ending in June, 1943, The Rockefeller Foundation distributed approximately seven and one-half million doses of this vaccine. The experience of The Foundation has also demonstrated the great benefits that can be derived by measures to eliminate the arthropod vectors that assist in the dissemination of certain viruses. A development of the war becomes of importance in this connection. The Army found a material, known as DDT, to be of great value in the control of an outbreak of typhus in Naples last year because of its lethal effect on the body louse, the arthropod vector of epidemic typhus. This or similar materials will probably be used in the future to control other arthropod vectors of disease agents. However, as was found to be the case with yellow fever, such measures will probably have to be supplemented with the use of adequate vaccines.

Outstanding successes have also been achieved in the control of certain virus diseases of animals by the use of vaccines containing active virus. The most important of these include hog cholera, fowl pox, laryngotracheitis of chickens, and ovine ecthyma of sheep and goats. In the immunization of swine against hog cholera, active virus is administered to the animal at one spot and immune serum is administered simultaneously at another spot. In the cases of the virus diseases of fowls, and ovine ecthyma of sheep, immunization is achieved by the administration of the active viruses by unnatural routes. The tremendous annual losses which used to occur in the swine, poultry and sheep industries have largely been eliminated because of the development of these effective vaccines. They are used on a scale little appreciated by the general public and have contributed greatly to the economy of the nation. I should perhaps mention that vaccines are not used in the control of virus diseases of plants. Such diseases are controlled by destroying the virus diseased plants as soon as possible and by the development of plant varieties that are resistant to virus diseases. In addition, heat treatment has effected cures in the case of certain plant virus diseases. Rigid quarantine measures established by the state and Federal governments have proved of

benefit in the control of many plant virus diseases. Quarantine measures have also proved useful in the control of certain animal virus diseases, for example foot-and-mouth disease of cattle in this country and rabies in England.

The fact that mutant strains of viruses are useful for purposes of immunization provides fascinating possibilities for the chemist, for as more and more is learned of the chemical structure peculiar to viruses, the better becomes the chance of altering a virus structure by means of definite chemical reactions with the formation of a new virus strain. The possibility exists, therefore, that at some time in the future the chemist may be able to produce by known chemical reactions definite virus strains for use in vaccines.

The second basic procedure which has proved useful in the conquest of virus diseases consists of vaccination with inactivated virus. This method has been exploited only recently, chiefly because of the general acceptance, for a great many years, of the idea that inactive virus fails to produce immunity. Nevertheless, the first example of the utilization of this method is probably furnished by Pasteur's experiments on rabies. Pasteur noted that the passage of rabies virus in rabbit brains caused a modification of the virus. However, in his classical immunization experiments, he vaccinated a given individual on the first day with a preparation obtained from a diseased rabbit cord that had been subjected to 14 days' desiccation, the next day with a preparation of a cord desiccated for 13 days, then with a 12-day cord and so on until the final vaccination was made with a preparation obtained from a freshly removed cord. He proved that the rabies virus in cords dried between 1 and 6 days was active. Although the cords dried for periods of time longer than about 6 to 8 days failed to produce the disease, it was thought, until recently, that they still contained a small amount of active virus. Now it seems possible that the initial immunity that was established and permitted the subsequent introduction of virus known to be active arose from the introduction of the inactive virus present in the 9- to 14-day cords. In recent years the idea that inactive virus can produce immunity has been accepted and it appears likely that the use of inactivated virus vaccines will be greatly increased in the future. Attempts to use this method for certain virus diseases have resulted in failures, but it has been used successfully in the cases of dog distemper and equine encephalomyelitis. It seems likely that the failures were due largely

to the use of inadequate amounts of inactivated virus or to destruction of the antigenicity of the virus during inactivation.

In many cases it has proved very difficult to secure large amounts of highly infectious diseased tissues for use in the preparation of vaccines. However, in 1931 there occurred a very important development which was destined to alter this picture considerably. In that year Woodruff and Goodpasture found that fowl pox virus would multiply within embryonated chicken eggs and since that time over 20 different viruses have been grown in chick embryos. Because of the ready availability of fertile chicken eggs, an almost inexhaustible source of these viruses thus became available. Today several active as well as inactive virus vaccines are prepared from viruses produced in chick embryos. Unfortunately even this rich source of virus appears to be inadequate in certain instances when the material is used directly. It is obvious that when vaccines consisting of inactive virus are used, they must contain a sufficient amount of immunizing antigen if they are to be successful. Fortunately viruses can be concentrated and it is possible that the concentration of viruses for use in the preparation of vaccines containing inactive virus will provide a new epoch in the conquest of certain virus diseases. One of these is influenza, a virus disease that was responsible for one of the three most destructive outbreaks of disease within the knowledge of man. During the influenza epidemic of 1918-19, approximately five hundred million people suffered from this disease, and of these approximately fifteen million died. At the height of the epidemic, one out of every fifty people in the world died each month, a death rate that is unsurpassed in history. During World War I no means of protection against influenza existed. Even the cause of the disease was unknown. Since then the virus of influenza has been discovered and it has been grown in chick embryos.

Events of major significance appear to be taking place in connection with the control of influenza, for an Army Commission ported in a recent number of the *Journal of the American Medical Association* that through the use of a concentrated vaccine prepared from the allantoic fluid of infected chick embryos the attack rate during an influenza epidemic was drastically reduced. It seems likely that progress will continue and that the concentration and purification of viruses by modern methods, such as differential centrifugation, will provide vaccines that will result in the elimination

of influenza and certain other virus diseases as major health problems. Thus, this type of biological engineering and vigorous, aggressive research on the viruses themselves should provide the means for the future conquest of virus diseases. The American pharmaceutical manufacturers can contribute greatly to this conquest by sponsoring research work on viruses in their own laboratories and in the laboratories of our universities. There is also a need for an awakening, on the part of the public, to the possibilities of research. Mankind's complacent and resigned acceptance of a world-wide catastrophe, such as the 1918 influenza epidemic, has been a source of wonderment to me. Here is a disease that in four months killed a half a million people in the United States alone, yet even the nature of the responsible infectious agent was unknown. Despite the tremendous destruction of human life by influenza, a destruction which in four months was far greater than that which resulted in years of combat activities in World War I, the annual monetary expenditure for searches for the true cause of the disease has probably been far less than the cost of a single bomber. The public should insist that the attack on these invisible agents of disease be pursued with the same vigor with which the attack on our visible enemies is now being made. Research is the foundation of this attack and with increased emphasis on research we will realize the true conquest of virus diseases.

APPETITE AND WALKING FAMINE

By T. Swann Harding

"A CHILD is a walking famine." This profound observation is attributed to Dr. Woods Hutchinson. The famous child specialist went on that the thing to do is simply feed a child wholesome food and let the "wisdom of the ages" operate. Under those circumstances you could trust the child with an open refrigerator or a candy box. The idea that the stomach requires a definite rest interval between operations was pronounced an exploded fallacy.

It is very doubtful, however, whether the average child would or could select for itself a well-balanced, nutritious diet if left free to choose among the sophisticated dishes that reach our tables. For, not only do children early acquire food prejudices; their perverted appetites are rarely guides to sound nutrition. Some hold that human beings have thus lost an attribute of the animals.

For the lower animals are said by many investigators wisely to correct their feed shortages, if fed proper diets, and to decrease or increase their general level of intake as is necessary. A good deal of evidence supports this contention as well as the theory that an animal's appetite is a sound instinctive guide to adequate rations.

Over a quarter of a century ago it was reported that rats used in experiments tended to take such foods as would promote their growth. They chose expertly between protein and nonprotein foods and could also distinguish high-grade, complete proteins from low-grade incomplete ones. They could more accurately select their own dietary protein levels than the technicians who worked with them, or so it was said.

Such rats would choose the good milk protein lactalbumin in preference to zein, the protein of corn, which is incomplete, even when the two were offered in pure form. They would eat enough to maintain good health and normal growth. Though they liked sugar they would not eat it in preference to a good protein like casein when they needed protein. They also chose vitamin-rich rather than vitamin-free foods.

If foods containing less valuable proteins were alone available they increased their intake so as to be sure of getting enough of this sparse constituent. We usually assume that a 14 per cent protein level is sufficient in a diet, but it is significant that the rats chose 30 per cent when this was available. Oddly enough, rabbits liked protein at that level too. They throve on a free food choice and gained weight faster and more economically than on any diet devised by their breeders.

Rats, in addition, were said to possess the power to detect and differentiate between small quantities of a poisonous substance like selenium in foodstuffs. If sublethal amounts of selenium were added to them, the rats voluntarily starved even when normal diets were offered them. The rats could also detect very slight differences in the selenium content of various diets offered them and would avoid those containing more and, if forced to do so, eat those containing least.

Even when synthetic foods were offered, alike in appearance and palatability, the rats would choose the nutrient optimum. They regarded alcohol as food too. Fed 8 per cent alcohol they reduced their food intake voluntarily and drank slightly less of the dilute alcohol available to them than they had of water previously. As the alcohol fed rose in percentage the food intake was still further reduced. They preferred weak concentrations of alcohol, and it replaced some food in their diets without untoward results.

If the adrenal glands are removed from rats they tend to die because of excessive loss of blood sodium in the urine. This changes the internal osmotic condition upon which life depends. But if salt is available the rats will persistently eat it in sufficient quantity to maintain life and health indefinitely.

Results with other animals are somewhat similar. Pigs deliberately prefer complete proteins. Their appetites are better guides to their bodily needs than pig growers ordinarily believe. Given good rations and plenty of salt, they grow more economically and efficiently than on human dietetic standards.

Pigs will balance their own rations if various feeds are offered in different compartments, lessening waste in food assimilation, and obtaining the highest energy value from their feed. What is really best for an animal may not, of course, suit a farmer's pocketbook or even his fancy, but a pig knows the best way of making a hog of himself nevertheless.

Dairy cows do not do so well, probably because they are really man-bred biological machines for milk production. They are not economical when self-fed and tend to overeat their maintenance and milk-production requirements. They usually consume excess energy, protein, or both. Their food preferences change from time to time and they are subject to whims. Some cows, for instance, turn out to be roughage drunks! However, when beef cattle are being fattened for market self-feeding works well. Cows also choose the better proteins when choice is permitted.

If the soil on which hay is grown is limed differently, some getting none and some getting considerable, with others in between, and the hay from these plots is then cut and stacked, dairy cattle select the high-calcium hay by preference. In fact, in one case where there were four stacks, the hay was consumed in the order of its calcium content, the high-calcium hay being eaten first.

Rats when stealing grain will also preferentially open bags which contain the grain with the highest calcium content, leaving the low-calcium grain bags untouched. Both animals could tell more about the food value of their feed than could be learned by genetic or chemical study of plant hybrids.

True, some doubts have been cast on work of this kind. Some investigators have contended that the better feeds or ration constituents must be distinguished by taste or smell before they are selected by preference. If they made the deficient diet taste and smell like the complete one the rats would eat it with continued relish.

In time, however, they would revert to the better diet even then. This was especially true when vitamins were being tested. It appeared that the animals could judge the value of diets, however, by observing their own recovery from the symptoms of malnutrition.

But self-knowledge or instinct seemed in abeyance in at least one experiment with rats. The main choice was between a diet of mineralized, vitamin-fortified skim-milk powder containing butter and an exactly similar diet wherein the fat was cottonseed, olive, corn, peanut or soybean oil, or margarine. Preferences were said to be associated with flavor.

The rats liked commercial butter flavor better than they did the flavor of natural butter which is based on its diacetyl content. Indeed they consistently chose the diet which was more palatable regardless of nutritive values. This experiment threw doubt on the

idea that rats could instinctively select adequate diets for normal growth and reproduction from a group of purified foodstuffs.

Though some of us are inclined to imagine that primitive men always arrived at adequate diets eventually by half instinctively making balanced mixtures of available foods, this is not true. Many tribes of primitives went undernourished and suffered from diseases like dental caries, rickets, mild scurvy, and beri beri associated with malnutrition.

On the other hand many primitives who were healthy in nature degenerated rapidly on the white man's diet. Though able to select a proper nutritive balance in their own environment they proved unable to do so in the white man's. Thus Bantu tribesmen of South Africa tend to live on partly cooked maize or mealie meal, sometimes supplemented with fermented cow's milk, and they have deficiency diseases in wide variety.

Rats fared no better than the Bantus on this diet. Their growth was retarded, their coats became poor, and they broke out with incrustations and other objectionable symptoms. This, of course, is why rats are so valuable in assaying the value of diets; they react to them so much like human beings.

Stories are in the literature about fowls, suffering from polyneuritis, who went on an exclusive diet of greens until cured, discarding cereal grains. On the other hand, we can find accounts of cows which refused limestone and bonemeal and unwisely stuck to salt, and of rats which failed to take sufficient protein to keep them alive when offered a good allowance of carbohydrates, proteins, and salts.

But nearly all investigators agree that animals have some ability to judge their own physical condition and to attribute their ills to a bad diet. If rats depleted of vitamin B are offered a choice between a diet devoid of that vitamin and a diet which contains it in very distinctive form, as in yeast or wheat germ, they will almost invariably choose the latter. If not depleted of the vitamin, however, they exhibit no preference until depleted.

A depleted rat will also continue indefinitely on the same monotonous diet containing a bare adequacy of the vitamin it requires rather than take novel diets devoid of that vitamin. If the vitamin-containing diet is placed before the rat in such quantities as to give

it an excess it will in time cease restricting itself to that diet. The rats here seem capable of self-education.

However, if a large number of different foods are placed before the rat, it will usually fail to discover the vitamin-containing diet. Yet, if a young rat is fed a vitamin-containing diet for a few days for educational purposes it will make a sound food selection when confronted with that diet later. Occasionally a smart rat will discover the correct diet from a large choice of foods and will adhere to it indefinitely.

If vitamins are incorporated in the food not from a natural source but in the form of the synthetic concentrates, rats tend to lose their power of discrimination. But if the vitamin-containing diet has a distinctive character with which the rat can associate the vitamin's presence, the animal's choice improves. Put the vitamin in the cocoa-flavored diet and get the rat to take it; then make the cocoa-flavored diet vitamin-free and you have the rat well fooled for a time, though capable of re-education.

It looks as if the ability of the vitamin-depleted rat to discriminate between diets is sometimes based rather upon the distinctive character of the diet than upon vague instinct. But the experience of getting beneficial results from certain diets also counts here. The rat is no fool—as anybody knows who ever tried to catch or poison one.

When it comes to children custom enters the picture. A child can be so accustomed to cod-liver oil that it will refuse jam unless a little cod-liver oil is added to "improve" the flavor. Such a child will also seek out and consume all the cod-liver oil in the house unless restrained. Usually children are early accustomed to sophisticated foodstuffs which trick whatever instinctive appetite food-selection apparatus they may have.

But, as Dr. Clara M. Davis has shown, veritable infants can be induced to select satisfactory diets if, when first weaned, they are confronted with a variety of simple foodstuffs from which it is possible for them to pick out adequate diets. In these circumstances natural appetite becomes an index of the wants of the system. The children thrive better and have fewer digestive disturbances than those fed as usual. Some of them have been followed on up into their teens and they turned out to be good physical specimens.

Mixed foods cannot be used, however—no breads, soups, or custards. But quite young infants can handle all natural foods eaten by

adults, including the muscle cuts of meat. All meats, fruits, and vegetables must be cut finely, whether raw or cooked. The infant's food choice must be absolute with no forcing from the attendant, no remonstrance, no commendation, no direction, no advice.

Foods are served on trays as usual and in customary containers, though in varied formation. The infants soon form habits and preferences. Later they promptly recognize and reach for foods they prefer. Some of the foods chosen are promptly spit out and they are rarely chosen again. On the other hand, since the foods are unsalted, and salt is served separately, the infants will bravely eat the salt though making faces and showing signs of displeasure.

The infants also go on food jags. Some will devour seven eggs or a half dozen bananas at a meal, disregarding all other foods. Others will stick exclusively to cereals, meats, or fruits for a while, increasing or decreasing their intake without ever having digestive disturbances. Beef is usually preferred raw or very rare. "Dunking" begins at 10 or 11 months of age, to soften crackers!

The infants take from 1,200 to 1,500 calories daily. They have good appetites, no digestive disturbances, no bowel complaints, no vomiting. Their growth and health are normal. Though just weaned, they can handle the normal natural foods in an adult diet without bad effects. When left to their own devices somewhat older children act similarly.

One group ranging in age from 6 to 13 was permitted to select their diet from a good basic diet. They could have as many portions as they wished of any food, provided they had cleaned up the first helping. But those who left food were not lectured; their portions simply became smaller next time. The children readily ate everything offered, but no untoward emotional situations were created by nagging or advising them.

The children unerringly selected proteins, calories, minerals, and vitamins in such quantities as to make up an adequate diet. Their selections ranged close to one another in percentage. Requirements set up by nutrition experts were well met. It was demonstrated that a well-rounded and intelligently formulated diet enables children to be their own guides as to quantities and specific foods eaten.

Dr. Davis also found the blood and bones of her infants in good shape. Their caloric intake was generally within limits prescribed by scientific nutrition. They tended towards alkaline-ash foods, and the

protein level of their diets ran from 9 to 20 per cent. They took fats and carbohydrates about as expert dietitians would prescribe, and their vitamins and minerals were well taken care of.

The Davis' kids started out by trying to eat everything offered. They took hopeful bites at the trays, chews of clean spoon, nibbles of dishes and paper napkins. They tried every food offered, restricting their diets later to what they liked. They expressed surprise, pleasure, or disgust at foods tasted, but they licked up the salt.

However, the child that breakfasted on a pint of orange juice and some raw liver came out well as did the one that insistently supped on several eggs, several bananas, and milk. Each achieved dietetic salvation by its own individual route. The whole trick here was to confine the infants to natural, unprocessed, unpurified foods, with no fancy dishes.

Adults do not do so badly, however. Several studies have shown that people in low-income classes generally incline to select diets as good as their pocketbooks afford. They take just about the calories and just about the mixture of proteins, fats, carbohydrates, minerals, and vitamins that scientific nutritionists would advise. They fall down when they cannot afford to buy sufficient of certain foods to balance their diets. One investigator wrote:

> "It seems that the normal woman has an instinctive knowledge of catering for her household and, though her instincts are not proof against sophistication and are much influenced by superstitions, prejudice and custom, it seems clear that education in dietetics properly given should produce an immediate response. This means that the application of theoretical dietetics will take care of itself, if the theory is taught in a way which is intelligible to those without scientific training."

It should be possible for us to use appetite as an instinctive guide rather more than we do. The great physiologist, Claude Bernard, had a theory that the organism instinctively seeks to maintain its stability by maintaining the stability of its internal environment. The use of appetite to procure a satisfactory diet is an instance of this.

A child is a walking famine in part because its food needs for growth are so overwhelming. It can rather easily be taught almost instinctively to balance its diet. This it can continue into adult life, the more easily, of course, if it avoids complicated, highly seasoned, complex sophisticated foods.

BIBLIOGRAPHY

Early work of Osborne and Mendel in many publications.

John M. Evvard: *Proc. Iowa Acad. Science 22*:375 (1915).

W. E. McCulloch: *West African Medical Journal 3*:1929 (via *Nature*, London, *127*:897-8, June 13, 1931).

J. B. Orr and J. L. Gilks: Medical Research Council Special Series No. 153, London.

Vilhjalmur Stefansson: *J. Amer. Dietetic Assn.*, July, 1937.

Journal American Medical Association, London Letter, *102*:383, Feb. 3, 1934, on Work of Dr. Leslie Harris of Cambridge, England.

W. B. Nevens: *University of Ill. Agr. Exp. Station Bull.* 289, May, 1927.

American J. Physiol., Dec. 1, 1921, p. 211.

Proc. Roy. Soc. 113:161, June 1, 1933.

Kurt W. Franke. *Science 83*:330ff, April 3, 1936.

Canadian Med. Assn. J., Sept., 1939, 257ff, v. 41, Clara M. Davis, M. D.

Quart. J. Studies on Alcohol 1:650-62, March, 1941.

Natl. Res. Council, Feb. 13, 1944, statement of Curt P. Richter before session of the Committee on Food Habits regarding work of William A. Albrecht and others; also an address by Albrecht before Department of Agriculture workers in 1944.

Christine Gilbert and Joseph Gillman: *Science 99*:398-9, May 19, 1944.

Magnus Pyke: *Nature* (London) August 19, 1944, 229-31, remarks on Curt Richter's work.

THE UNITED STATES AS THE NEW CENTER FOR THE STUDY OF THE HISTORY OF PHARMACY

By Henry Colle

EVEN before the outbreak of the current World War, Europe had declined as a center for the Study of the History of Pharmacy. The advent of Hitler as Chancellor of Germany in 1933 signalled the death knell of such studies in that country. Germany, which had been world famous for its scholars in this field, with its noted families of pharmacists, the Gmelin and other noted names, its Societies for the Study of the History of Pharmacy, declined rapidly. Liberals, and scholars of every stripe were proscribed. A pall settled over the land as though a plague of locusts sought to deprive it of intellectual sanity.

But proscription was not enough for the mad fanatics who took over the destinies of the European continent. An orgy of cruelty was unloosed, and scholars formerly proscribed were ruthlessly herded to internment camps. Rumor was soon replaced by fact. A stench arose from central Europe where the charnel houses were worked overtime—a stench that hangs in the nostrils of every decent man—as the terrifying names of Oswiecim, Lublin, Klooga (White Russia), and other places are mentioned, together with the awful facts which have been reported by credible observers in such magazines as *Life, Time,* and the *Saturday Evening Post,* and which now find confirmation by the United States Government and the report of the United States War Refugee Board.

These sadistic acts of cruelty are mentioned here only to show how futile it is to expect any recrudescence from these avauntedly hallowed precincts of culture in Central Europe.

Then Leipzig was bombed. According to a report in the magazine *Nation,* the bombing was part of the United Nations' plan for the systematic destruction of the German war industries. Leipzig had the greatest book industry in Europe. Its reputation was centuries old, but it had war industries, too. The bombing was necessary. But the greatest collection of trade libraries, catering to scholars, since the Alexandrian Libraries, was wiped out.

It is true that there are many great book centers beside Leipzig in the world today. But none exhibited the "know-how" of book

manufacturing for the sciences as did Leipzig in the last several centuries. Its loss is a prodigious one but it may well be counted a gain, if it helps to curb the savagery which has been unleashed over Central Europe.

American Scholars and Scholarship

From this introduction we turn to our own country, and the American background in pharmaceutical history. We can turn our backs on Europe, even though the older generation of scholars obtained its training there.

Generally speaking, however, such American studies as have entered into the History of Pharmacy, are connected with local scenes. Notable is the "History of Pharmacy in the United States," by Kremers and Urdang.

There are histories of colleges, State Associations, and local pharmaceutical bodies, as well as numberless sketches of American pharmacists.

American Studies in the Field of International Pharmacy

LaWall's "Four Thousand Years of Pharmacy," is one of the few international essays by a historian of Pharmacy in the United States, as is the "History of Pharmacy" by Kremers and Urdang. Another work along the same lines is the writer's own "Social and Cultural Aspects of Pharmacy, Vol. 1 and 2," published in hectograph and copyrighted in 1942.

Of American scholars' efforts in the field of the History of Pharmacy, be it said (and it is true of this field as of many others) too few scholars are producing too much. They are overworked in trying to revive interest and keep interest from flagging in this field of pharmaceutical research.

Outstanding contemporary names in the study of the History of Pharmacy are George Urdang, Director of the American Institute of the History of Pharmacy (Madison, Wis.); Dr. Wulling, Dean Emeritus of the University of Minnesota College of Pharmacy; Otto Raubenheimer, retail pharmacist of Brooklyn, N. Y., and author of many articles for the old *Druggists Circular* circa 1932; L. E. Warren, who presented an outstanding lecture on Pharmacy and Medicine of Ancient Egypt, before the General Session of the American Pharmaceutical Association at Miami, Florida in 1931 and which was published in the *Journal* of the Association in the October, 1931, issue.

The Society for the Study of the History of Science

A great aid to the interested historian of Science and Pharmacy is the History of Science Society. This noted organization for research in the History of Science maintains as its organ a journal known as *ISIS*. The bibliography of works published in the field of the History of Science appears in one of the quarterly issues. This is a "must" for every serious student in this field. The bibliography mentions works published in the History of Pharmacy and related fields. Dr. George Sarton, Professor of the History of Science at Harvard University, is the editor.

Library Facilities and the Study of the History of Pharmacy

The History of Pharmacy, like all other scientific pursuits, demands access to adequate library facilities.

In this respect pharmacy in its historical aspects seems to be the tail to the kite of historical medicine. Obviously, there is need for change.

In the opinion of the writer, were the funds and facilities available, the best places for the establishment of such research centers are San Francisco and Los Angeles in the Pacific Coast area, Detroit and Chicago in the Midwest, and Philadelphia, Boston, and New York in the East.

These cities are named because of their proximity to established libraries.

The prospects for large independently controlled pharmaceutical libraries is not bright. Scholars would do best to work with already established libraries, such as in

San Francisco, the Sutro Branch of the California State Library which has a fine collection of Hebrew manuscripts and works;

Pasadena, near Los Angeles, Calif.—The Huntington Library, strong in Americana and incunabula or works published prior to the fifteenth century;

Chicago—Center of the great libraries on the Near East, connected with the University of Chicago;

Detroit—To be the center of a great multi-million dollar medical center and also the home of the famous Hooker scientific library;

Philadelphia—Contains a score or more of libraries, such as the American Philosophical Society, the Academy of Sciences, the Philadelphia College of Pharmacy and Science and others;

New York—Wherein may be found the treasure house of the New York Public Library and similar institutions;

Washington, D. C.—The Library of Congress, which is one of the ten greatest in the world.

Various Fields Making Up the History of Pharmacy

Today the Study of the History of Pharmacy ranks among its scholars research specialists, who bridge the whole field, and who, because they are pioneers amidst an abundance of riches, feel impelled to call to the attention of the casual onlooker the vast panorama as a whole.

But following these are the specialists hewing to the line, as, for instance, one in the Islamic field for research, rich with such names as Ibn Sina, or Avicenna, Al-Beitar, Al-Rhazes, and others.

Then there is the Chinese field, with the so-called Famine Herbals, a phenomena peculiar to China, wherein are described roots, barks, herbs, flowers, etc., which the Chinese in their ageless fight against war and famine have found useful. There is the allied field of Indian or Hindu Pharmacy, with the great names of Sushruta and Charaka, barely known to the West, but affecting western medicine more than we realize.

There is the great field of Hebraic medicine, with such giants as Maimonides, the great Jewish physician to the Court of Saladin, in Islam's heyday. He wrote prolifically in the field of pharmacy and medicine.

Another is the Western European field of Pharmacy—its medieval aspects, and the part the Renaissance played, with such notables as Paracelsus, Albertus Magnus and others.

Reverting to a more remote period is the Pharmacy of Ancient Egypt, the Ebers Papyrus and its disclosures, Assyria and its traditions. A vast field of study opens here.

S. N. Kramer, a noted Assyriologist, indeed the greatest living authority on Sumerian mythology, who is connected with the University of Pennsylvania, has just published a work on the "Mythology of Sumer." It details, in a fashion that is easy for the non-specialist

to follow, the history of the uncovering of Sumeria, the predecessor peoples of the Assyrians, and he traces the origins of Assyriological studies in this country from their inception, and their contacts with European scholarship. All this is grist for the scholar's mill.

Peace Treaties Should Guarantee Access to European Libraries

European, especially central European libraries, have had the reputation of guarding their treasures jealously. A condition of the peace treaties, when war is ended on the European continent, should include free access to, and use of, enemy libraries, under conditions which would preclude hardships to American and allied scholars.

History of Pharmacy Is Deserving of Full Professorial Rank

The Study of the History of Pharmacy is deserving of full professorial rank. Its present status of an elective subject, in most colleges, is not satisfactory.

The eminent French historian Taine is said to have remarked that if the cadaver is the subject for pathological study of man, then the history of a nation is determinative of its current outlook, and a similar analogy could be held for a craft or profession. The great heights to which Pharmacy can achieve in the world of Today, and Tomorrow, cannot be fully visualized if we do not adequately study its Yesterday.

Equally unsatisfactory is the teaching of the subject by professors of pharmacy, who teach it as an adjunct to another subject, such as practical pharmacy, without the necessary background.

Conclusion

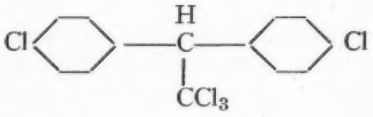
However, there is an optimistic outlook to the problem, for prospects are bright for improvement in conditions under which the Study of the History of Pharmacy will be taught. As requirements for pharmaceutical studies are raised, it will be discerned that the present becomes tomorrow's history, and the historical process and its importance in Pharmacy will be fully recognized.

With the destruction of the centers of history in Europe, the task falls upon those in America. There is no doubt but that we shall measure up to the challenge.

SELECTED ABSTRACTS

The New Insecticide: Some Properties of D. D. T. (Editor). *Pharm. J. 99,* 256 (1944). D. D. T. is the abbreviation of the chemical name *p*-dichloro-diphenyl-trichloroethane, or more completely, aá-bis-(*p*-chlorophenyl)-βββ-trichloroethane. This compound, synthesized by a German chemist in 1874, escaped attention as an insecticide until a Swiss company only quite recently patented its use for that purpose. About December, 1942, British and American investigators began tests which showed its remarkable insecticidal properties.

D. D. T. can be prepared by condensing chlorobenzene with chloral in the presence of sulfuric monohydrate. Its structural formula is as follows:



It is a white powder with a slightly sweet odor; it is soluble in organic solvents but insoluble in water. The compound is not affected by light, air or water, and it can be used in emulsions without loss of efficiency. Surfaces coated with a film of D. D. T. are poisonous to insects which walk over them, remaining so for at least three months. Clothing impregnated with it remains safe from infestation by lice for a month, despite several launderings.

D. D. T. has been found to kill a great variety of insects and thus gives promise of a wide application for domestic, agricultural and horticultural uses. The compound was highly successful in controlling an outbreak of typhus in Naples in 1943, and it has been extensively used in the military campaigns, especially in tropical regions. It was observed that the application of a solution of 10 per cent D. D. T. and 5 per cent cyclohexanone in kerosene in a house infested with bedbugs caused death among these insects for as long as 104 days thereafter.

Experiments have shown that the incorporation of 5 per cent of D. D. T. in oil-bound water paints renders a painted surface lethal to flies which come in contact with it for at least two months and only slightly less effective after six months. The compound also is efficient when contained in a coumarone resin film or in a wax floor polish. White lead oil paints and synthetic varnish enamels containing D. D. T. do not, however, exhibit insecticidal properties.

In the dry form or as an aqueous suspension D. D. T. is almost harmless to man, though precautions should be observed to prevent undue inhalation of the dry dust or fine spray. Military medical authorities recommend that solutions of the compound in organic solvents should be handled only by trained personnel properly protected against prolonged exposure of the skin to such solutions.

Investigations of the toxicity of D. D. T. administered orally to experimental animals have shown that the compound produces tremors, spasticity and terminal extensor rigidity, with only slight histological changes in the central nervous system. The most marked pathological alteration consisted of a degeneration of the liver cells. Such evidence of toxicity, coupled with the observations that D. D. T. is cumulative in its action and that it is absorbable through the skin, emphasizes the need for caution in handling it.

Acute Toxicity of Commercial Penicillin. H. Welsh, C. W. Price, J. K. Neilsen and A. C. Hunter. *J. Lab. &Clin. Med. 29,* 809 (1944); through *U. S. Nav. Med. Bull. 43,* 908 (1944). A wide variation was observed in the acute toxicity of over 300 lots of penicillin sodium produced by fourteen manufacturers, although all lots passed the mouse safety test. Some products were lethal for mice in concentrations of 3,500 to 5,000 units; one brand of penicillin sodium was lethal only in doses of 25,000 to 32,000 units.

A comparison of commercial samples of the calcium and sodium salts of penicillin revealed that the former is much more toxic, but the authors contend that this fact should not discourage the clinical use of the calcium salt in man.

The toxicity of high potency samples of penicillin sodium and high or low potency samples of penicillin magnesium is primarily due to the cation used in producing these preparations, and the same explanation applies to the calcium and ammonium salts.

Sulfa-Mercury Compound for Venereal Prophylaxis. J. F. Blute, Jr. *U. S. Nav. Med. Bull. 43,* 1063 (1944). An effective prophylaxis against venereal disease among Naval personnel must be (1) simple, requiring no elaborate apparatus to make or to administer; (2) easily available both to ships and shore establishments; (3) non-irritating and not painful or toxic; and (4) effective in preventing disease.

This paper reports the use of such a prophylactic solution in a series of 80 consecutive cases aboard ship. Its use was instituted when it became evident that preparations containing calomel and silver compounds failed to offer protection. In the cases cited, not a single case of venereal disease resulted; in contrast, during the same period, 16 cases of gonorrhea, 3 cases of lymphogranuloma, and 1 case of syphilis were noted among men who either took no prophylaxis or used the calomel and silver method.

The formula for the preparation is as follows:

Mercury oxycyanide	0.20
Sulfathiazole powder	10.00
Tragacanth	10.00
Water	225.00

The three powders are mixed, after which the water is gradually added and incorporated by mixing with a spatula. The finished preparation has the character of an emulsion and should have a heavy creamy consistency such that it can easily be aspirated and ejected through a penile syringe.

About 5 cc. of the product is introduced into the urethra and retained for 5 minutes by the clock. After the material has been removed as completely as possible, the urethra is washed out with a syringeful of liquid petrolatum. The prophylactic should not be retained longer than 5 minutes since a painful chemical urethritis results on longer contact.

BOOK REVIEWS

Bacteriology and Allied Subjects. By Louis Gershenfeld, B. Sc., Ph. M., D. Sc., Professor of Bacteriology and Hygiene and Director of the Bacteriological Laboratories at the Philadelphia College of Pharmacy and Science. 585 pp. Mack Publishing Co. $6.00.

The author's qualifications to prepare a book on this subject can best be described by naming a few of the important positions that he holds which are directly related to applied bacteriology. Dr. Greshenfeld is chairman of the National Formulary Subcommittee on Clinical Laboratory Preparations, and also on subcommittees responsible for Bacteriological and Biological Preparations and Bacteriological Media. He is a member of the U. S. P. Sterile Products Advisory Board, Secretary of the National Biological Stain Commission, an Associate Editor of the United States Dispensatory and a collaborating author of a number of other authoritative texts.

This new book by Dr. Gershenfeld should not be considered as simply a revision of his earlier work "Bacteriology and Sanitary Science." It is much more comprehensive in scope and entirely rewritten. The text is divided into seven parts as follows:

I. Bacteriology.
II. The Higher Bacteria, Fungi, Rickettsiæ and Filterable Viruses.
III. Sterilization and Disinfection.
IV. Animal Parasitology.
V. Insect Control, Insecticides and Fumigation.
VI. Immunity, Allergy and Biological Products.
VII. Applied Bacteriology.

A number of aspects of the book are unique and in some instances not to be found in any other book on this subject. As examples of the above we might mention a chronological list of the discovery of microorganisms causing disease, a full chapter devoted to the preparation of all important culture media, a discussion of industrial processes involving bacterial action, the use of ultra-violet rays in sterilization, the preparation of sterile products, an excellent presentation of biological products and complete technics for the sanitary examination of water, dairy products, foods, etc.

The author has prepared this book particularly for those who are engaged in the pharmaceutical or some related field, since so many textbooks of bacteriology present the subject only from the standpoint of bacteriology as a basic science.

To all such persons the book should prove a most valuable reference and it is undoubtedly an ideal text for students majoring in pharmacy.

The publishers are to be complimented for the excellent printing and binding to be observed in this book. L. F. TICE.

Fundamental Principles and Processes of Pharmacy. By H. M. Burlage, Ph. D., with J. B. Burt, Ph. D., C. O. Lee, Ph. D., and L. W. Rising, Ph. D., as collaborators. First Edition. 615 pp., incl. index. McGraw-Hill. $4.50.

This is a new book in the field of pharmacy and its primary objective is to serve as a textbook for the beginning student in pharmacy. The book is arranged in the same sequence as that course prescribed in the Pharmaceutical Syllabus bearing the same name. Since Dr. Burlage is chairman of the National Pharmaceutical Syllabus Committee such a book under his capable editorship is quite logical.

The arrangement of the text follows rather closely the sequence used by most teachers of pharmacy in giving to freshman students an introduction to their professional study and a proper orientation so that they may understand the courses that lie ahead, their professional responsibilities and, finally, the processes and technics involved in the practice of pharmacy.

The authors have done a commendable job in the preparation of this book and its chapters are well organized and clearly written. The text is well illustrated with both drawings and photographs and this is particularly valuable to the student. The chapter on "The Natural Products Used in Pharmacy" would have been better omitted since it is quite impossible to present this material in the thirty-seven pages devoted to it. The book would not have suffered in any way if this had been done, inasmuch as it is not the purpose of this text to cover medicinal agents.

Your reviewer who teaches the subject matter presented in this book considers it an excellent textbook and well worth the attention of pharmaceutical educators. L. F. TICE.

Here are 19 prescription specialties you can count on for prestige, profit, and *real demand* during 1945.

These outstanding products of Schering research ... embracing sulfonamides, X-Ray contrast media, an antacid, a gold salt, and a comprehensive group of hormones in various dosage forms... will be heavily advertised to physicians during the coming year.

And *heavily advertised* means *heavily prescribed.*

SCHERING CORPORATION • Bloomfield, N. J.

An Education in

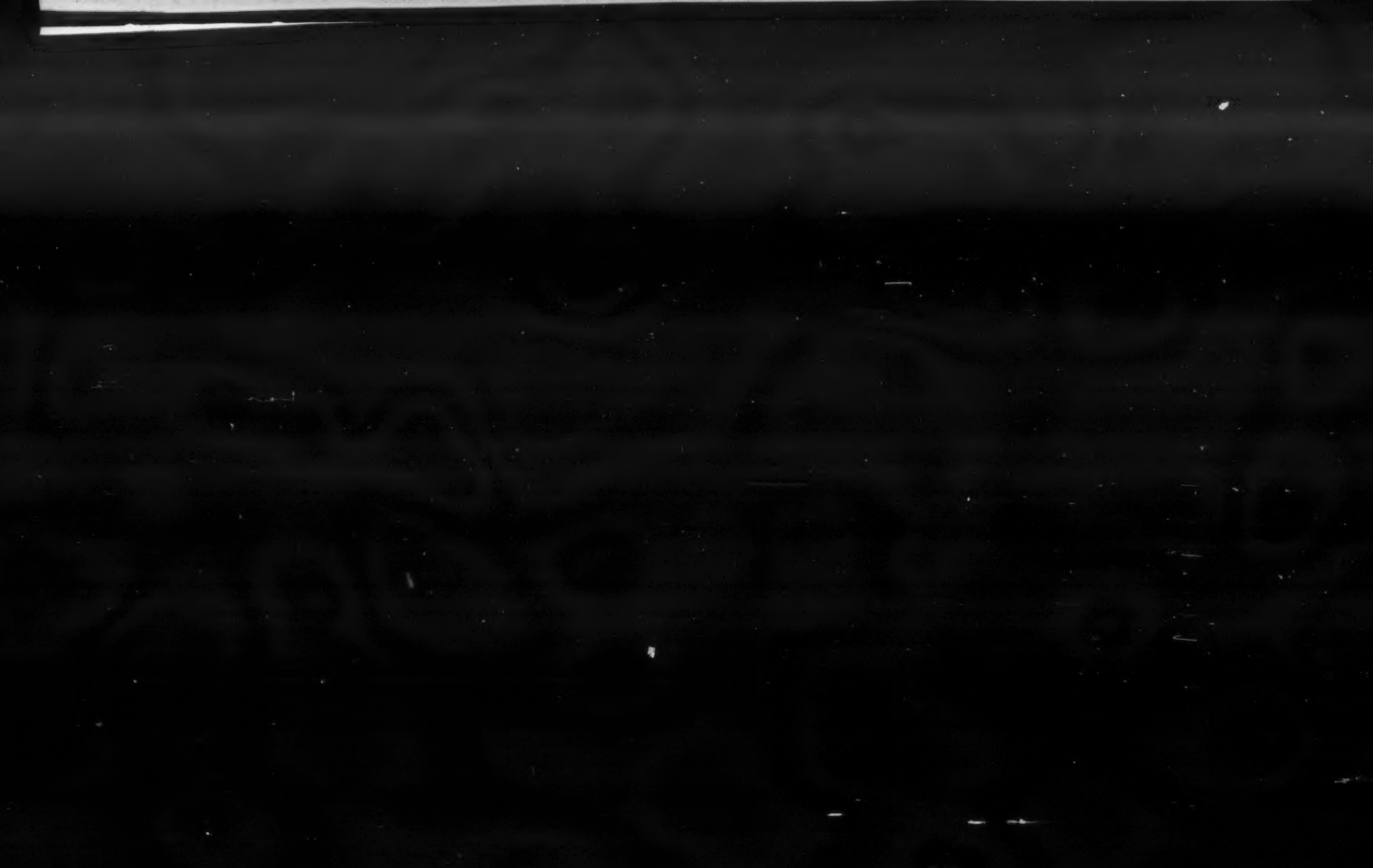
PHARMACY OR ALLIED SCIENCES

YOUNG men and women find opportunities for successful careers in pharmacy, chemistry, bacteriology and biology, following education in this institution. B. Sc. degree courses. Modern buildings, complete equipment, coeducational. Classes begin September 20. Inquiries from returning Service men invited. Write for catalog.

Philadelphia College of Pharmacy and Science

43rd Street, Kingsessing and Woodland Avenues,
Founded 1821

Philadelphia 4 Pennsylvania



American Journal of Pharmacy

The American Journal of Pharmacy is the oldest continuously published scientific periodical of its kind in America, having been established by the Philadelphia College of Pharmacy in 1825. After the original issue there were three other preliminary numbers until 1829, when regular publication began. From then until 1852 four issues were published annually, with the single exception of 1847, when an additional number appeared. Six issues a year were printed from 1853 to 1870, at which time the Journal became a monthly publication.

Former Editors of the Journal have been: Daniel B. Smith, 1825-1828; Benjamin Ellis, 1829-1831; Robert E. Griffith, 1831-1836; Joseph Carson, 1836-1850; William Procter, Jr., 1850-1871; John M. Maisch, 1871-1893; Henry Trimble, 1893-1898; Henry Kraemer, 1898-1917; George M. Beringer, 1917-1921, and Ivor Griffith, 1921-1941.

Established and maintained as a record of the progress of pharmacy and the allied sciences, the Journal's contents and policies are governed by an Editor and a Committee on Publications elected by the members of the College.

Manuscripts should be sent to the Editor, who does not assume any responsibility in connection with the views or investigations of contributors of accepted manuscripts, other than to exercise general care in selection.

Contributors are allowed a reasonable number of copies of this Journal, free of charge, if applied for when the proof is returned.

Reprints, if desired, should be ordered when the proof is returned. The table below shows the *approximate* cost of reprints, the make-up of the pages to be identically the same as in the Journal. The actual cost may vary from the figures given, and will depend upon the amount of presswork, paper, binding, and other factors. Reprints containing half-tones may be expected to cost somewhat more than the rates given.

	2 pp.	4 pp.	8 pp.	16 pp.	Covers with Titles
50 copies.....	$3.50	$6.00	$10.50	$11.25	50 copies $5.00
100 "	4.25	7.00	14.00	15.00	100 " 6.50
250 "	5.25	9.00	18.75	20.00	250 " 10.25

Popular Science Talks

IN BOOK FORM

Interesting ● Readable ● Dependable

In 1921 a series of free evening lectures on science for the general public was inaugurated by the members of the Faculty of the Philadelphia College of Pharmacy and Science. The series was continued for many years thereafter, with an annual change in the topics of the talks.

The lectures were designed to convey a maximum of scientific information on timely subjects, yet using a minimum of technical language.

After the lectures had been delivered, there was a demand for the talks in book form. Fourteen such volumes have been issued to date, but only ten remain in print. They are used by many high schools as reference books. Libraries have them available. Science teachers and lecturers find them useful. The complete set is a valuable addition to any library, public or private. The books serve admirably as gifts.

All of the books are paper-bound. The price for each is $1, post-paid. Orders are honored promptly.

Send for a descriptive booklet

American Journal of Pharmacy

43rd Street, Kingsessing and Woodland Avenues

PHILADELPHIA 4, PENNSYLVANIA